AGGCGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGAATGGACTGGCCTCACAACCTGCTGTTTCTT
CTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAAGAGGAAGGGGCAAGGGCG
GCCTGGGCCCTGGCCCTCACCAGGTGCCACTGGACCTGGTGTCACGGATGAAACCGTATGCCC
GCATGGAGGAGTATGAGAGGAACATCGAGGAGATGGTGGCCCAGCTGAGGAACAGCTCAGAGCTGGCCCAG
AGAAAGTGTGAGGTCAACTTGCAGCTGTGGATGTCCAACAAGAGGAGCCTGTCTCCCTGGGGCTACAGCAT
CAACCACGACCCCAGCCGTATCCCCGTGGACCTGCCGGAGGCACGGTGCCTGTGTCTCGGGCTGTGAACC
CCTTCACCATGCAGGAGACCGCAGCATGGTGAGCGTGCCGGTGTTCAGCCAGGTTCCTGTGCGCCGCCGC
CTCTGCCCGCCACCGCCCCCCCACAGGGCCTTGCCGCCAGCGCCAGCTCATGGAGACCATCGCTGTGGGCTG
CACCTGCATCTTCTGAATCACCTGGCCCAGAAGCCAGGCCAGCACCCCGAGACCATCCTTTTCACCCTTT

 ${\tt MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEEYERNIEEMVA} \\ QLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGCVNPFTMQEDRSMVSVP\\ VFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF$ 

MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPHLLARGAKWGQALPVALVSSLE AASHRGRHERPSATTQCPVLRPEEVLEADTHQRSISPWRYRVDTDEDRYPQKLAFAECLCRGCIDARTGRE TAALNSVRLLQSLLVLRRRPCSRDGSGLPTPGAFAFHTEFIHVPVGCTCVLPRSV

Signal peptide:

Tyrosine kinase phosphorylation site:

N-myristoylation sites:

Leucine zipper pattern:

Homologous region to IL-17:

Amino acids 1-18

Amino acids 112-121

Amino acids

32-38;55-61;133-139

Amino acids 3-25

Amino acids 99-195

GTGCCCGACTTGTGACTGAGTGTGCAGTGCCCAGCATGTACCAGGTCAGTGCAGAGGGCTGCCTGAGGGCT GTGCTGAGAGGGAGGAGCAGAGATGCTGCTGAGGGTGGAGGCCAAGCTGCCAGGTTTGGGGCTGG  $\tt GGGCCAAGTGGAGTGAGAAACTGGGATCCCAGGGGGAGGGTGCAG\underline{ATG}AGGGAGCGACCCAGATTAGGTGA$  $\tt GGACAGTTCTCATTAGCCTTTTCCTACAGGTGGTTGCATTCTTGGCAATGGTCATGGGAACCCACACCT$ ACAGCCACTGGCCCAGCTGCCCCCAGCAAAGGGCAGGACACCTCTGAGGAGCTGCTGAGGTGGAGCACT GTGCCTGTGCCTCCCCTAGAGCCTGCTAGGCCCAACCGCCACCCAGAGTCCTGTAGGGCCAGTGAAGATGGA  $\tt CCCCTCAACAGCAGGCCCATCTCCCCCTGGAGATATGAGTTGGACAGAGACTTGAACCGGCTCCCCCAGGA$ GCAACTCGGAGCTGCTCTACCACAACCAGACTGTCTTCTACAGGCGGCCATGCCATGGCGAGAAGGGCACC GATGGGCTAGCCGGACCTGCTGGAGGCTGGTCCCTTTTTGGGAAACCTGGAGCCAGGTGTACAACCACTTG CCATGAAGGGCCAGGATGCCCAGATGCTTGGCCCCTGTGAAGTGCTGTCTGGAGCAGCAGGATCCCGGGAC AGGATGGGGGGCTTTGGGGAAAACCTGCACTTCTGCACATTTTGAAAAGAGCAGCTGCTGCTTAGGGCCGC  $\tt CGGAAGCTGGTGTCCTGTCATTTTCTCTCAGGAAAGGTTTTCAAAGTTCTGCCCATTTCTGGAGGCCACCA$ CTCCTGTCTCTTCCTCTTTTCCCATCCCCTGCTACCCTGGCCCAGCACAGGCACTTTCTAGATATTTCCCC  $\tt CTTGCTGGAGAAGAAGAGCCCCTGGTTTTATTTGTTTACTCATCACTCAGTGAGCATCTACTTTGG$ GTGCATTCTAGTGTAGTTACTAGTCTTTTGACATGGATGATTCTGAGGAGGAAGCTGTTATTGAATGTATA GAGATTTATCCAAATAAATATCTTTATTTAAAAATGAAAAA

 ${\tt MRERPRLGEDSSLISLFLQVVAFLAMVMGTHTYSHWPSCCPSKGQDTSEELLRWSTVPVPPLEPARPNRHP}$ ESCRASEDGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDPRGNSELLYHNQTVFYR RPCHGEKGTHKGYCLERRLYRVSLACVCVRPRVMG

Signal peptide:

Amino acids 1-32

N-glycosylation site:

Amino acids 136-140

Tyrosine kinase phosphorylation site: Amino acids 127-135

N-myristoylation sites:

Amino acids 44-50;150-156

**ATG**CTGGTAGCCGGCTTCCTGCTGCGCCCGAGCTGGGCCGCGGGCGCCCCCAGGCCGGCAGGCC CCCCGCGCGCCGCGGGCTGCGCGGACCGGCCGGAGGAGCTACTGGAGCAGCTGTACGGGCGCCTGGCGG CCGGCGTGCTCAGTGCCTTCCACCACACGCTGCAGCTGGGGCCGCGTGAGCAGGCGCGCAACGCGAGCTGC CCGGCAGGGGCAGGCCCGGCGACCGCCGCTTCCGGCCGCCCACCAACCTGCGCAGCGTGTCGCCCTGGGC ${\tt GCCTGACCGGGCTGTTCGGCGAGGAGGACGTGCGCTTCCGCAGCGCCCCTGTCTACATGCCCACCGTCGTC}$  $\tt CTGCGCCGCACCCCGCCTGCGCCGGCGGCCGTTCCGTTACACCGAGGCCTACGTCACCATCCCCGTGGG$ CTGCACCTGCGTCCCCGAGCCGGAGAAGGACGCAGACATCAACTCCAGCATCGACAAACAGGGCGCCCA AGCTCCTGCTGGGCCCCAACGACGCCCCGCTGGCCCCTGAGGCCGGTCCTGCCCCGGGAGGTCTCCCCGG GAGCAAACCAAGTGCCGGAGCACCAGCGCCCTTTCCATGGAGACTCGTAAGCAGCTTCATCTGACACGG GCATCCCTGGCTTGCTTTTAGCTACAAGCAAGCAGCGTGGCTGGAAGCTGATGGGAAACGACCCGGCACGG GCATCCTGTGTGCGGCCCGCATGGAGGGTTTGGAAAAGTTCACGGAGGCTCCCTGAGGAGCCTCTCAGATC  $\tt GGCTGCTGCGGGTGCAGGGCGTGACTCACCGCTGGGTGCTTGCCAAAGAGATAGGGACGCATATGCTTTTT$ AAAGCAATCTAAAAATAATAATAAGTATAGCGACTATATACCTACTTTTAAAATCAACTGTTTTGAATAGA  ${\tt GGCAGAGCTATTTTATATTATCAAATGAGAGCTACTCTGTTACATTTCTTAACATATAAACATCGTTTTTT}$ ACTTCTTCTGGTAGAATTTTTTAAAGCATAATTGGAATCCTTGGATAAATTTTGTAGCTGGTACACTCTGG TTCCTTCCACTGAAGGTCTTCACGGGCCTCCAGGTGGACCAAAGGGATGCACAGGCGGCTCGCATGCCCCA GGGCCAGCTAAGAGTTCCAAAGATCTCAGATTTGGTTTTAGTCATGAATACATAAACAGTCTCAAACTCGC ACAATTTTTTCCCCCTTTTGAAAGCCACTGGGGCCAATTTGTGGTTAAGAGGTGGTGAGATAAGAAGTGGA  ${\tt ACGTGACATCTTTGCCAGTTGTCAGAAGAATCCAAGCAGGTATTGGCTTAGTTGTAAGGGCTTTAGGATCA}$ GGCTGAATATGAGGACAAAGTGGGCCACGTTAGCATCTGCAGAGATCAATCTGGAGGCTTCTGTTTCTGCA AAAAGTTAGTAGTTCTTTTTAAATCATTAAAAGAGGCTTGCTGAAGGAT

MLVAGFLLALPPSWAAGAPRAGRRPARPRGCADRPEELLEQLYGRLAAGVLSAFHHTLQLGPREQARNASC PAGGRPGDRRFRPPTNLRSVSPWAYRISYDPARYPRYLPEAYCLCRGCLTGLFGEEDVRFRSAPVYMPTVV LRRTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSINSSIDKQGAKLLLGPNDAPAGP

Signal peptide:

Amino acids 1-15

N-glycosylation sites:

Amino acids 68-72;181-185

Tyrosine kinase phosphorylation site:

Amino acids 97-106

N-myristoylation sites:

Amino acids 17-23;49-55;74-80;

118-124

Amidation site:

Amino acids 21-25

# FIGURE 9

# FIGURE 10

 ${\tt MTVKTLHGPAMVKYLLLSILGLAFLSEAAARKIPKVGHTFFQKPESCPPVPGGSMKLDIGIINENQRVSMS} \\ RNIESRSTSPWNYTVTWDPNRYPSEVVQAQCRNLGCINAQGKEDISMNSVPIQQETLVVRRKHQGCSVSFQ\\ LEKVLVTVGCTCVTPVIHHVQ$ 

Signal sequence:

Amino acids 1-30

N-glycosylation site:

Amino acids 83-86

N-myristoylation sites:

Amino acids 106-111;136-141

# FIGURE 11

 $\tt CCGGCG\underline{ATG} \\ TCGCTCGTGCTAAGCCTGGCCGCTGTGCAGGAGCGCCGTACCCGAGAGCCGACCGT$ TCAATGTGGCTCTGAAACTGGGCCATCTCCAGAGTGGATGCTACAACATGATCTAATCCCCGGAGACTTGA GGGACCTCCGAGTAGAACCTGTTACAACTAGTGTTGCAACAGGGGACTATTCAATTTTGATGAATGTAAGC TGGGTACTCCGGGCAGATGCCAGCATCCGCTTGTTGAAGGCCACCAAGATTTGTGTGACGGGCAAAAGCAA  $\tt CTTCCAGTCCTACAGCTGTGAGGTGCAATTACACAGAGGCCTTCCAGACTCAGACCCAGACCCTCTGGTG$ GTAAATGGACATTTTCCTACATCGGCTTCCCTGTAGAGCTGAACACAGTCTATTTCATTGGGGCCCATAAT ATTCCTAATGCAAATATGAATGAAGATGGCCCTTCCATGTCTGTGAATTTCACCTCACCAGGCTGCCTAGA CCACATAATGAAATATAAAAAAAAGTGTGTCAAGGCCGGAAGCCTGTGGGGATCCGAACATCACTGCTTGTA AGAAGAATGAGGAGACAGTAGAAGTGAACTTCACAACCACTCCCCTGGGAAACAGATACATGGCTCTTATC GGTGATTCCAGTGACTGGGGATAGTGAAGGTGCTACGGTGCAGCTGACTCCATATTTTCCTACTTGTGGCA GCGACTGCATCCGACATAAAGGAACAGTTGTGCTCTGCCCACAAACAGGCGTCCCTTTCCCTCTGGATAAC  ${\tt AACAAAGCAAGCCGGGAGGCTGCCTGCTCTCCTCCTGCTGCTGCTGGTGGCCACATGGGTGCTGGT}$  $\tt GGCAGGGATCTATCTAATGTGGAGGCACGAAAGGATCAAGAAGACTTCCTTTTCTACCACCACCACTACTGC$ CCCCCATTAAGGTTCTTGTGGTTTACCCATCTGAAATATGTTTCCATCACACAATTTGTTACTTCACTGAA TTTCTTCAAAACCATTGCAGAAGTGAGGTCATCCTTGAAAAGTGGCAGAAAAAGAAAATAGCAGAGATGGG  ${\tt ACAGTGTGCGATGGTACCTGTGGCAAGAGCGAGGGCAGTCCCAGTGAGAACTCTCAAGACCTCTTCCCC}$ CTTGCCTTTAACCTTTTCTGCAGTGATCTAAGAAGCCAGATTCATCTGCACAAATACGTGGTGGTCTACTTTAGAGAGATTGATACAAAAGACGATTACAATGCTCTCAGTGTCTGCCCCAAGTACCACCTCATGAAGGATG CCACTGCTTTCTGTGCAGAACTTCTCCATGTCAAGCAGCAGGTGTCAGCAGGAAAAAGATCACAAGCCTGC CACGATGGCTGCTGCTCCTTGTAG

# FIGURE 12

MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLIPGDLRDLRVEPVTTSVATGDYSILMNVSWV LRADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTRPSGGKWTFSYIGFPVELNTVYFIGAHNIP NANMNEDGPSMSVNFTSPGCLDHIMKYKKKCVKAGSLWDPNITACKKNEETVEVNFTTTPLGNRYMALIQH STIIGFSQVFEPHQKKQTRASVVIPVTGDSEGATVQLTPYFPTCGSDCIRHKGTVVLCPQTGVPFPLDNNK SKPGGWLPLLLLSLLVATWVLVAGIYLMWRHERIKKTSFSTTTLLPPIKVLVVYPSEICFHHTICYFTEFL QNHCRSEVILEKWQKKKIAEMGPVQWLATQKKAADKVVFLLSNDVNSVCDGTCGKSEGSPSENSQDLFPLA FNLFCSDLRSQIHLHKYVVVYFREIDTKDDYNALSVCPKYHLMKDATAFCAELLHVKQQVSAGKRSQACHD GCCSL

Signal sequence:

Amino acids 1-14

Transmembrane domain:

Amino acids 290-309

N-glycosylation sites:

Amino acids 67-70;103-106;156-159;

183-186;197-200;283-286

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 228-231;319-322

N-myristoylation site:

Amino acids 116-121

Amidation site:

Amino acids 488-491

## FIGURE 13

ACACTGGCCAAACAAAAACGAAAGCACTCCGTGCTGGAAGTAGGAGGAGGAGTCAGGACTCCCAGGACAGAG AGTGCACAAACTACCCAGCACAGCCCCCTCCGCCCCCTCTGGAGGCTGAAGAGGGATTCCAGCCCCTGCCA  $\texttt{GCCACCTGGCACCTAGAAG} \underline{\textbf{ATG}} \texttt{CCTGTGCCCTGGTTCTTGCTGTCCTTGGCACTGGGCCGAAGCCCAGTGG}$ TCCTTTCTCTGGAGAGGCTTGTGGGGCCTCAGGACGCTACCCACTGCTCTCCGGGCCTCTCCTGCCGCCTC TGGGACAGTGACATACTCTGCCTGCCTGGGGACATCGTGCCTGCTCCGGGCCCCGTGCTGGCGCCTACGCA ACTTGGCCGTGCATGGGCACTGGGAAGAGCCTGAAGATGAGGAAAAGTTTGGAGGAGCAGCTGACTCAGGG GTGGAGGAGCCTAGGAATGCCTCTCCCAGGCCCAAGTCGTGCTCTCCTTCCAGGCCTACCCTACTGCCCG  $\tt CTGCGTCCTGCTGGAGGTGCAAGTGCCTGCTGCCCTTGTGCAGTTTGGTCAGTCTGTGGGCTCTGTGGTATAT$ GACTGCTTCGAGGCTGCCCTAGGGAGTGAGGTACGAATCTGGTCCTATACTCAGCCCAGGTACGAGAAGGA ACTCAACCACACACAGCAGCTGCCTGCCCTGCCCTGGCTCAACGTGTCAGCAGATGGTGACAACGTGCATC TGGTTCTGAATGTCTCTGAGGAGCAGCACTTCGGCCTCTCCCTGTACTGGAATCAGGTCCAGGGCCCCCCA AAACCCCGGTGGCACAAAAACCTGACTGGACCGCAGATCATTACCTTGAACCACACAGACCTGGTTCCCTG CCTCTGTATTCAGGTGTGGCCTCTGGAACCTGACTCCGTTAGGACGAACATCTGCCCCTTCAGGGAGGACC GGTCCCACCGCTTTCCTGGGAGAACGTCACTGTGGACAAGGTTCTCGAGTTCCCATTGCTGAAAGGCCACC CTAACCTCTGTGTTCAGGTGAACAGCTCGGAGAAGCTGCAGCTGCAGGAGTGCTTGTGGGCTGACTCCCTG GGGCCTCTCAAAGACGATGTGCTACTGTTGGAGACACGAGGCCCCCAGGACAACAGATCCCTCTGTGCCTT GGAACCCAGTGGCTGTACTTCACTACCCAGCAAAGCCTCCACGAGGGCAGCTCGCCTTGGAGAGTACTTAC TACAAGACCTGCAGTCAGGCCAGTGTCTGCAGCTATGGGACGATGACTTGGGAGCGCTATGGGCCTGCCCC CCTCATCCTCCTTCTCAAAAAGGATCACGCGAAAGGGTGGCTGAGGCTCTTGAAACAGGACGTCCGCTCGG GGGCGCCGCCAGGGGCCGCGCGCTCTGCTCCTCTACTCAGCCGATGACTCGGGTTTCGAGCGCCTGGTG GGCGCCCTGGCGTCGGCCCTGTGCCAGCTGCCGCTGCGCGTGGCCGTAGACCTGTGGAGCCGTCGTGAACT GAGCGCGCAGGGGCCCGTGGCTTGGTTTCACGCGCAGCGCGCCAGACCCTGCAGGAGGGCGCGTGGTGG TCTTGCTCTTCTCCCGGTGCGGTGGCGCTGTGCAGCGAGTGGCTACAGGATGGGGTGTCCGGGCCCGGG GCGCACGGCCCGCACGACGCCTTCCGCGCCTCGCTCAGCTGCTGCCCCGACTTCTTGCAGGGCCGGGC GCCCGGCAGCTACGTGGGGGGCCTGCTTCGACAGGCTGCTCCACCCGGACGCCGTACCCGCCCTTTTCCGCA CCGTGCCGTCTTCACACTGCCCCAACTGCCAGACTTCCTGGGGGCCCTGCAGCAGCCTCGCGCCCCG CCATCCCCGGGGACTCCCGCGCGGGACGCGGGGTGGGACCAGGGGCGGGACCTGGGGCGGGGACGGGA CTTAAATAAAGGCAGACGCTGTTTTTCTAAAAAAA

## FIGURE 14

MPVPWFLLSLALGRSPVVLSLERLVGPQDATHCSPGLSCRLWDSDILCLPGDIVPAPGPVLAPTHLQTELV  $\tt LRCQKETDCDLCLRVAVHLAVHGHWEEPEDEEKFGGAADSGVEEPRNASLQAQVVLSFQAYPTARCVLLEV$  ${\tt QVPAALVQFGQSVGSVVYDCFEAALGSEVRIWSYTQPRYEKELNHTQQLPALPWLNVSADGDNVHLVLNVS}$ EEQHFGLSLYWNQVQGPPKPRWHKNLTGPQIITLNHTDLVPCLCIQVWPLEPDSVRTNICPFREDPRAHQN LWOAARLRLLTLOSWLLDAPCSLPAEAALCWRAPGGDPCQPLVPPLSWENVTVDKVLEFPLLKGHPNLCVQ VNSSEKLOLOECLWADSLGPLKDDVLLLETRGPQDNRSLCALEPSGCTSLPSKASTRAARLGEYLLQDLQS GQCLQLWDDDLGALWACPMDKYIHKRWALVWLACLLFAAALSLILLLKKDHAKGWLRLLKQDVRSGAAARG  ${\tt RAALLLYSADDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAWFHAQRRQTLQEGGVVVLLFSP}$ GAVALCSEWLQDGVSGPGAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLLHPDAVPALFRTVPVFT LPSQLPDFLGALQQPRAPRSGRLQERAEQVSRALQPALDSYFHPPGTPAPGRGVGPGAGPGAGDGT

signal sequence:

Amino acids 1-20

transmembrane domain:

Amino acids 453-473

N-glycosylation sites:

Amino acids 118-121;186-189;198-201;

211-214;238-241;248-251;334-337;

357-360;391-394

Glycosaminoglycan attachment site: Amino acids 583-586

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 552-555

N-myristoylation sites:

Amino acids 107-112;152-157;319-324;

438-443;516-521;612-617;692-697;

696-701;700-705

## FIGURE 15

 $\texttt{CCATGTTCCGGGAGCCCTAATTGCACAGAAGCCC} \underline{\textbf{ATG}} \\ \texttt{GGGAGCTCCAGACTGGCAGCCCTGCTCCTGCCTC} \\$ TCCTCCTCATAGTCATCGACCTCTCTGACTCTGCTGGGATTGGCTTTCGCCACCTGCCCCACTGGAACACC CGCTGTCCTCTGGCCTCCCACACGGATGACAGTTTCACTGGAAGTTCTGCCTATATCCCTTGCCGCACCTG GTGGGCCCTCTTCTCCACAAAGCCTTGGTGTGTGCGAGTCTGGCACTGTTCCCGCTGTTTGTGCCAGCATCTGC TGTCAGGTGGCTCAGGTCTTCAACGGGGCCTCTTCCACCTCCTGGTGCAGAAATCCAAAAAGTCTTCCACA TGAGAAGAGCCATCACATTTCCATCCCCTCCCCAGACATCTCCCACAAGGGACTTCGCTCTAAAAGGACCC AACCTTCGGATCCAGAGACATGGGAAAGTCTTCCCAGATTGGACTCACAAAGGCATGGAGGACCCGAGTTC TCCTTTGATTTGCTGCCTGAGGCCCGGGCTATTCGGGTGACCATATCTTCAGGCCCTGAGGTCAGCGTGCG TCTTTGTCACCAGTGGGCACTGGAGTGTGAAGAGCTGAGCAGTCCCTATGATGTCCAGAAAATTGTGTCTG GAGGACACTGTGAGGCGCAAAAAATGTCCCTTCCAGAGCTGGCCAGAAGCCTATGGCTCGGACTTCTGGAA GTCAGTGCACTTCACTGACTACAGCCAGCACACTCAGATGGTCATGGCCCTGACACTCCGCTGCCCACTGA AGCTGGAAGCTGCCCTCTGCCAGAGGCACGACTGGCATACCCTTTGCAAAGACCTCCCGAATGCCACGGCT  $\tt CGAGAGTCAGATGGGTGGTATGTTTTGGAGAAGGTGGACCTGCACCCCAGCTCTGCTTCAAGTTCTCTTT$ TGGAAACAGCAGCCATGTTGAATGCCCCCACCAGACTGGGTCTCTCACATCCTGGAATGTAAGCATGGATA  $\tt CCAGGCTTGGGGCAGGACACTTTGGTGCCCCCGTGTACACTGTCAGCCAGGCCCGGGGCTCAAGCCCAGT$ GTCACTAGACCTCATCATTCCCTTCCTGAGGCCAGGGTGCTGTGTCCTGGTGTGGCGGTCAGATGTCCAGT TTGCCTGGAAGCACCTCTTGTGTCCAGATGTCTCTTACAGACACCTGGGGCTCTTGATCCTGGCACTGCTG GCCCTCCTCACCCTACTGGGTGTTGTTCTGGCCCTCACCTGCCGGCGCCCACAGTCAGGCCCGGGCCCAGC  $\tt GCTGCCCGCGCCGCTGCTGCTGCTCGCTTACTTCAGTCGCCTCTGCGCCAAGGGCGACATCCCCCCGCC$ AGCCGGCTTGAACGAGAGGCCGCCGACTTGCAGACCTAGGTTGAGCAGAGCTCCACCGCAGTCCCGGGTGTCT

## FIGURE 16

MGSSRLAALLLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFTGSSAYIPCRTWWALFSTKPWCV RVWHCSRCLCQHLLSGGSGLQRGLFHLLVQKSKKSSTFKFYRRHKMPAPAQRKLLPRRHLSEKSHHISIPS PDISHKGLRSKRTQPSDPETWESLPRLDSQRHGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQWALECE ELSSPYDVQKIVSGGHTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQH TOMVMALTLRCPLKLEAALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQLCFKFSFGNSSHVECPH OTGSLTSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQARGSSPVSLDLIIPFLR  $\tt PGCCVLVWRSDVQFAWKHLLCPDVSYRHLGLLILALLALLTLLGVVLALTCRRPQSGPGPARPVLLLHAAD$ SEAORRLVGALAELLRAALGGGRDVIVDLWEGRHVARVGPLPWLWAARTRVAREQGTVLLLWSGADLRPVS GPDPRAAPLLALLHAAPRPLLLLAYFSRLCAKGDIPPPLRALPRYRLLRDLPRLLRALDARPFAEATSWGR LGARQRRQSRLELCSRLEREAARLADLG

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 455-472

N-glycosylation sites:

Amino acids 318-322;347-351;364-368

Glycosaminoglycan attachment site: Amino acids 482-486

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 104-108;645-649

Tyrosine kinase phosphorylation site:

Amino acids 322-329

N-myristoylation sites:

Amino acids 90-96;358-364;470-476

Eukaryotic cobalamin-binding proteins:

Amino acids 453-462

## FIGURE 17

GAAACAGTGGGCTGTACAACATCACCTTCAAATATGACAATTGTACCACCTACTTGAATCCAGTGGGGAAG CATGTGATTGCTGACGCCCAGAATATCACCATCAGCCAGTATGCTTGCCATGACCAAGTGGCAGTCACCAT TCTTTGGTCCCCAGGGGCCCTCGGCATCGAATTCCTGAAAGGATTTCGGGTAATACTGGAGGAGCTGAAGT CGGAGGGAAGACAGTGCCAACAACTGATTCTAAAGGATCCGAAGCAGCTCAACAGTAGCTTCAAAAGAACT  $\tt GGAATGGAATCTCAACCTTTCCTGAATATGAAATTTGAAACGGATTATTTCGTAAAGGTTGTCCCTTTTCC$ TTCCATTAAAAACGAAAGCAATTACCACCCTTTCTTCTTTAGAACCCGAGCCTGTGACCTGTTGTTACAGC AGGTGTCCTTCGACCACGCACGCATGGCTCGGACATGCAGGTGTCCTTCGACCACGCACCGCACAACTTC GGCTTCCGTTTCTTCTATCTTCACTACAAGCTCAAGCACGAAGGACCTTTCAAGCGAAAGACCTGTAAGCA GGAGCAAACTACAGAGATGACCAGCTGCCTCCTTCAAAATGTTTCTCCAGGGGATTATATAATTGAGCTGG TGGATGACACTAACACAACAAGAAAAGTGATGCATTATGCCTTAAAGCCAGTGCACTCCCCGTGGGCCGGG  $\tt CCCATCAGAGCCGTGGCCATCACAGTGCCACTGGTAGTCATATCGGCATTCGCGACGCTCTTCACTGTGAT$ GTGCCGCAAGAAGCAACAAGAAAATATATATTCACATTTAGATGAAGAGAGCTCTGAGTCTTCCACATACA  $\tt CTGCAGCACTCCCAAGAGAGGGCTCCGGCCGGCCGAAGGTCTTTCTCTGCTATTCCAGTAAAGATGGC$ CAGAATCACATGAATGTCGTCCAGTGTTTCGCCTACTTCCTCCAGGACTTCTGTGGCTGTGAGGTGGCTCT GGACCTGTGGGAAGACTTCAGCCTCTGTAGAGAAGGGCAGAGAAATGGGTCATCCAGAAGATCCACGAGT CCCAGTTCATCATTGTGGTTTGTTCCAAAGGTATGAAGTACTTTGTGGACAAGAAGAACTACAAAACACAAA GGAGGTGGCCGAGGCTCGGGGAAAGGAGAGCTCTTCCTGGTGGCGGTGTCAGCCATTGCCGAAAAGCTCCG CCAGGCCAAGCAGAGTTCGTCCGCGGCGCTCAGCAAGTTTATCGCCGTCTACTTTGATTATTCCTGCGAGG GAGACGTCCCCGGTATCCTAGACCTGAGTACCAAGTACAGACTCATGGACAATCTTCCTCAGCTCTGTTCC CACCTGCACTCCCGAGACCACGGCCTCCAGGAGCCGGGGCAGCACACGCGACAGGGCAGCAGAAGGAACTA  $\tt CTTCCGGAGCAAGTCAGGCCGGTCCCTATACGTCGCCATTTGCAACATGCACCAGTTTATTGACGAGGAGC$ CCGACTGGTTCGAAAAGCAGTTCGTTCCCTTCCATCCTCCACTGCGCTACCGGGAGCCAGTCTTGGAG AAATTTGATTCGGGCTTGGTTTTAAATGATGTCATGTGCAAACCAGGGCCTGAGAGTGACTTCTGCCTAAA GGTAGAGGCGGCTGTTCTTGGGGCAACCGGACCAGCCGACTCCCAGCACGAGAGTCAGCATGGGGCCTGG ACCAAGACGGGGAGGCCCGGCCTGCCCTTGACGGTAGCGCCGCCCTGCAACCCCTGCTGCACACGGTGAAA  $\tt GCCGGCAGCCCTCGGACATGCCGCGGGACTCAGGCATCTATGACTCGTCTGTGCCCTCATCCGAGCTGTC$ TCTGCCACTGATGGAAGGACTCTCGACGGACCAGACAGAAACGTCTTCCCTGACGGAGAGCGTGTCCTCCT GATCTTGGTTGCCGCAGCTACACTGATGAACTCCACGCGGTCGCCCCTTTGTAACAAAACGAAAGAGTCTA 

# FIGURE 18

MPRASASGVPALFVSGEQGVGPASRNSGLYNITFKYDNCTTYLNPVGKHVIADAQNITISQYACHDQVAVT
ILWSPGALGIEFLKGFRVILEELKSEGRQCQQLILKDPKQLNSSFKRTGMESQPFLNMKFETDYFVKVVPF
PSIKNESNYHPFFFRTRACDLLLQPDNLACKPFWKPRNLNISQHGSDMQVSFDHAPHGSDMQVSFDHAPHN
FGFRFFYLHYKLKHEGPFKRKTCKQEQTTEMTSCLLQNVSPGDYIIELVDDTNTTRKVMHYALKPVHSPWA
GPIRAVAITVPLVVISAFATLFTVMCRKKQQENIYSHLDEESSESSTYTAALPRERLRPRPKVFLCYSSKD
GQNHMNVVQCFAYFLQDFCGCEVALDLWEDFSLCREGQREWVIQKIHESQFIIVVCSKGMKYFVDKKNYKH
KGGGRGSGKGELFLVAVSAIAEKLRQAKQSSSAALSKFIAVYFDYSCEGDVPGILDLSTKYRLMDNLPQLC
SHLHSRDHGLQEPGQHTRQGSRRNYFRSKSGRSLYVAICNMHQFIDEEPDWFEKQFVPFHPPPLRYREPVL
EKFDSGLVLNDVMCKPGPESDFCLKVEAAVLGATGPADSQHESQHGGLDQDGEARPALDGSAALQPLLHTV
KAGSPSDMPRDSGIYDSSVPSSELSLPLMEGLSTDQTETSSLTESVSSSSGLGEEEPPALPSKLLSSGSCK
ADLGCRSYTDELHAVAPL

Transmembrane domain:

Amino acids 283-307

N-glycosylation sites:

Amino acids 31-34;38-41;56-59;

113-116;147-150;182-185;266-269

Glycosaminoglycan attachment sites: Amino acids 433-436;689-692

cAMP- and cGMP-dependent protein kinase phosphorylation:
Amino acids 232-235

Tyrosine kinase phosphorylation sites:

Amino acids 312-319;416-424

N-myristoylation site:

Amino acids 19-24;375-380;428-433;

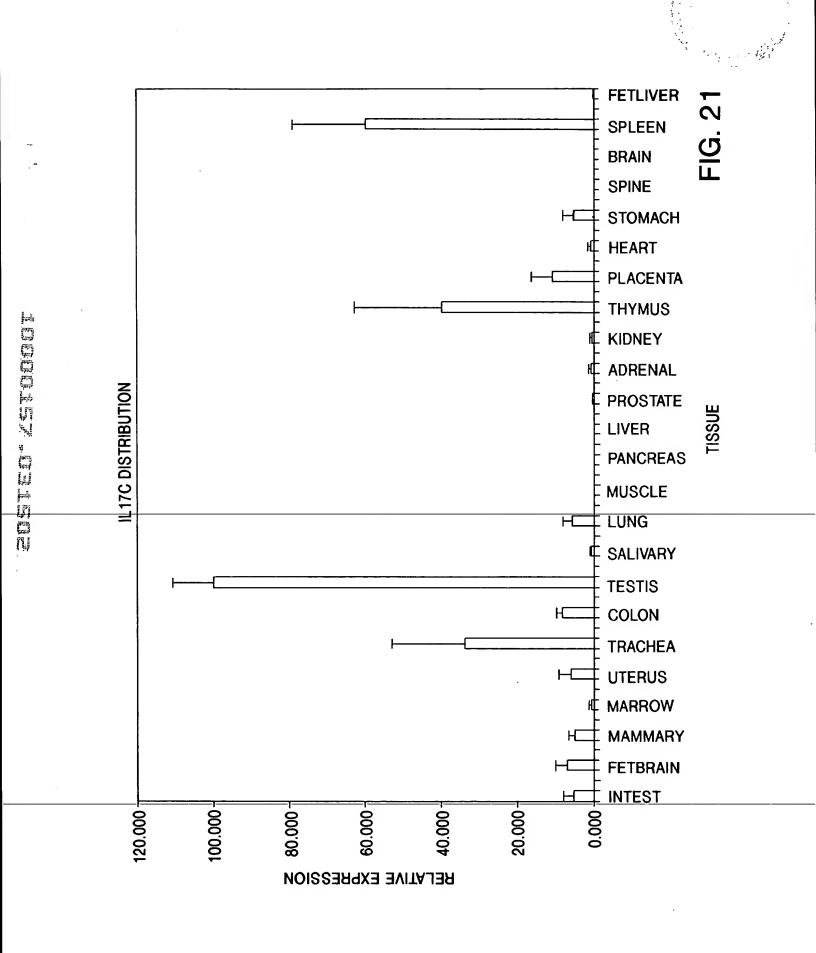
429-434;432-437;517-522;574-579;

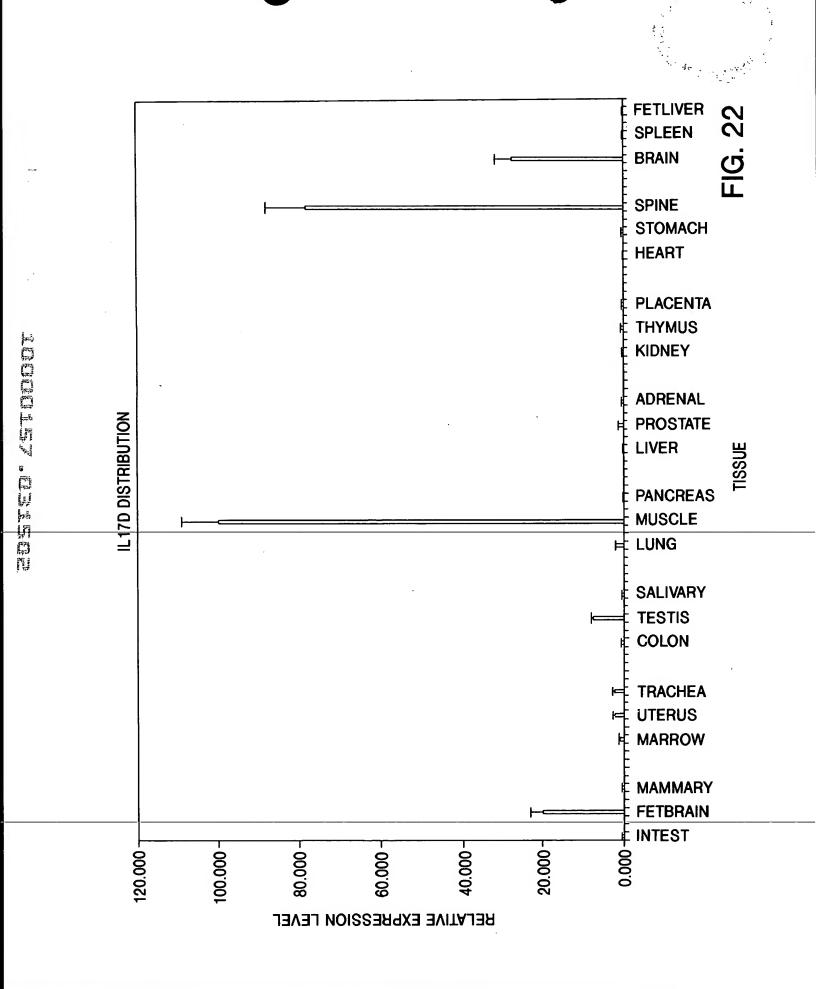
652-657;707-712

THE POLITION OF THE POLITION O	A P G C P N S E D K N F P B T V M V N L N I H N B N T N T N P K B S S D H Q V P L D L V S B M K P Y A R M E E Y E R N I E E M V A Q L R N S E L A Q R K C E V N L Q L W M L A R G A K W G Q A L P V A L V S S L E A A S H R G R H E R P S A T T Q C P V L R P E E V L E A D B B F R P P E E L L E Q L Y G R L A A G V L S A F H H T L Q L G P R E Q A R N A S C P A G G R P A D R R F R P P N P S C C P S K G Q D T S E E L L R W S T V P V P P L E P A R P N R H P E S C R A S E D G P A T F F Q K P E S C P V P G G S M K L D I G I I N E N Q R V S	Y N R S T S P WN L H R N E D P E R Y P S V I WE A K C R H L G C I N A D - G N V D Y H M N S V P S N K R S L S P W G Y S I N H D P S R I I P V D L P E A R C L C L G C V N P F T M Q E D R S M V S V P F T H Q R S I S P W R Y R V D T D E D R Y P Q X L A F A E C L C R G C I D A R T G R E T A A L N S V R F N S A P F N S A P F N S A P R I S Y D P A R Y P R Y L P E A Y C L C R G C L T G L F G E E D V R F R S A P F R S A P F S R S T S P W R Y E L D R D L N R L P Q D L Y H A R C L C P H C V S L Q T G S H M D P R G N S E I E S R S T S P W N Y T V T W D P N R Y P S E V V Q A Q C R N L G C I N A Q - G K E D I S M N S V P	V F S Q V P V R R R L C P P P · · · · · · P R T G P C R Q R A V M E T I A V G C T C V T P I V H H V A L L Q S L L V L R R R P C S R D G S G L P T P G A F A F H T E F I H V P V G C T C V L P R S V · · · · · · · G R S V Y E A Y V T I P V G C T C V L P R S V · · · · · · · G R S V Y T E A Y V T I P V G C T C V L P R P E R E K D A D L L Y H N Q T V F Y R R P C H G E K · · G T H K G Y C L E R R L Y R V S L A C V C V R P R V M G · · · · · · · · · · · · · · · · · ·
1 1	0	66 Y Y N R 101 T H Q R R 86 T N L R R 82 L N S R R 74 L E S R	115   Q   Q   E 143 V F S Q 151 L L   Q S 136 V Y M P 132 L L Y H 123   Q   Q   E
h-IL.17B h-IL.17B h-IL.17C h-IL.17D h-IL.17E h-IL.17E	h-IL17 h-IL17B h-IL17C h-IL17D h-IL17E h-IL17F	h-IL178 h-IL178 h-IL17C h-IL17C h-IL17E h-IL17E	h-IL17B h-IL17C h-IL17C h-IL17E h-IL17E

FIG. 19

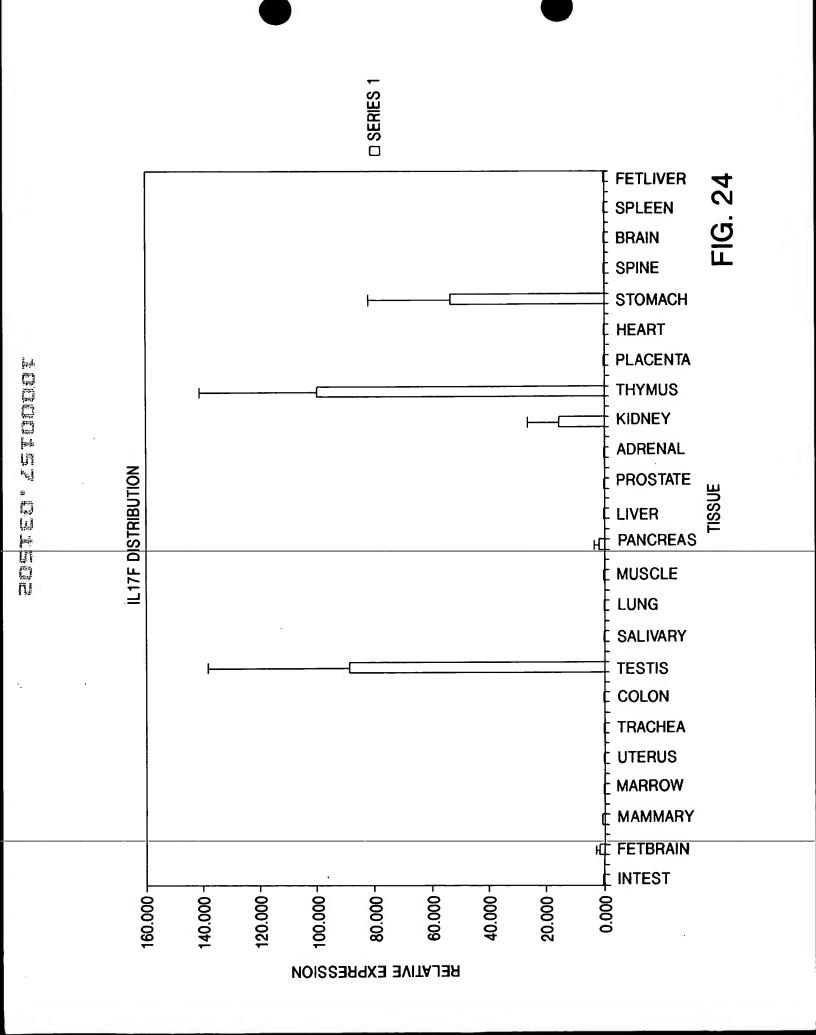
h-11.17D

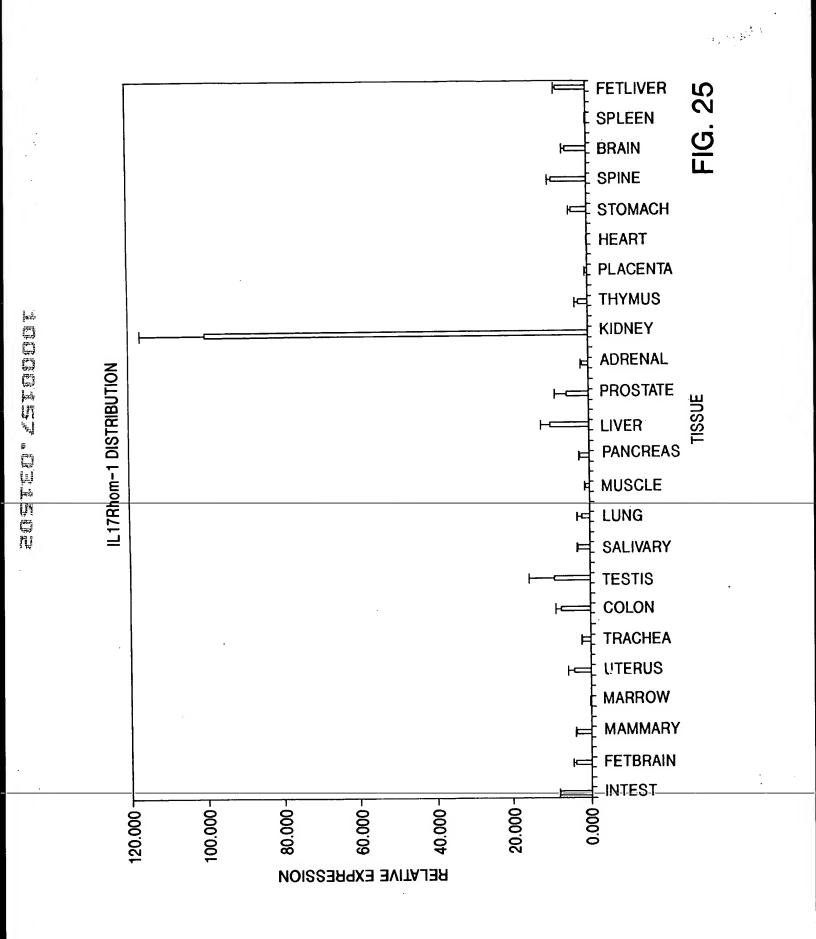


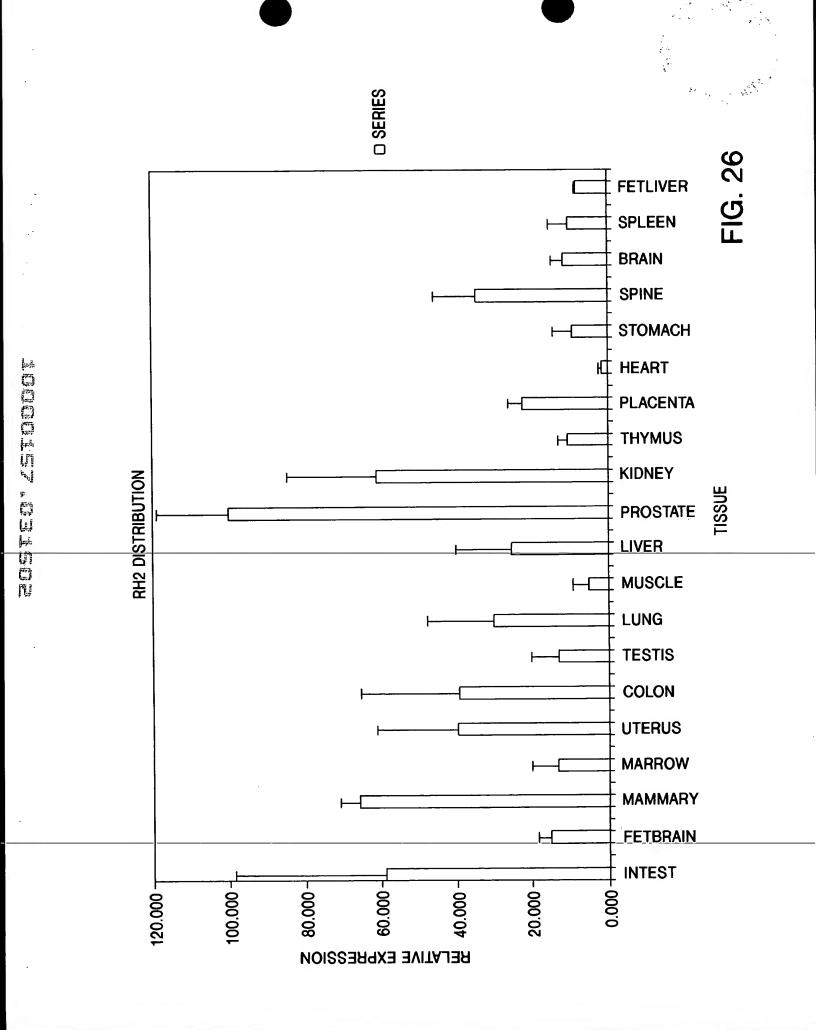


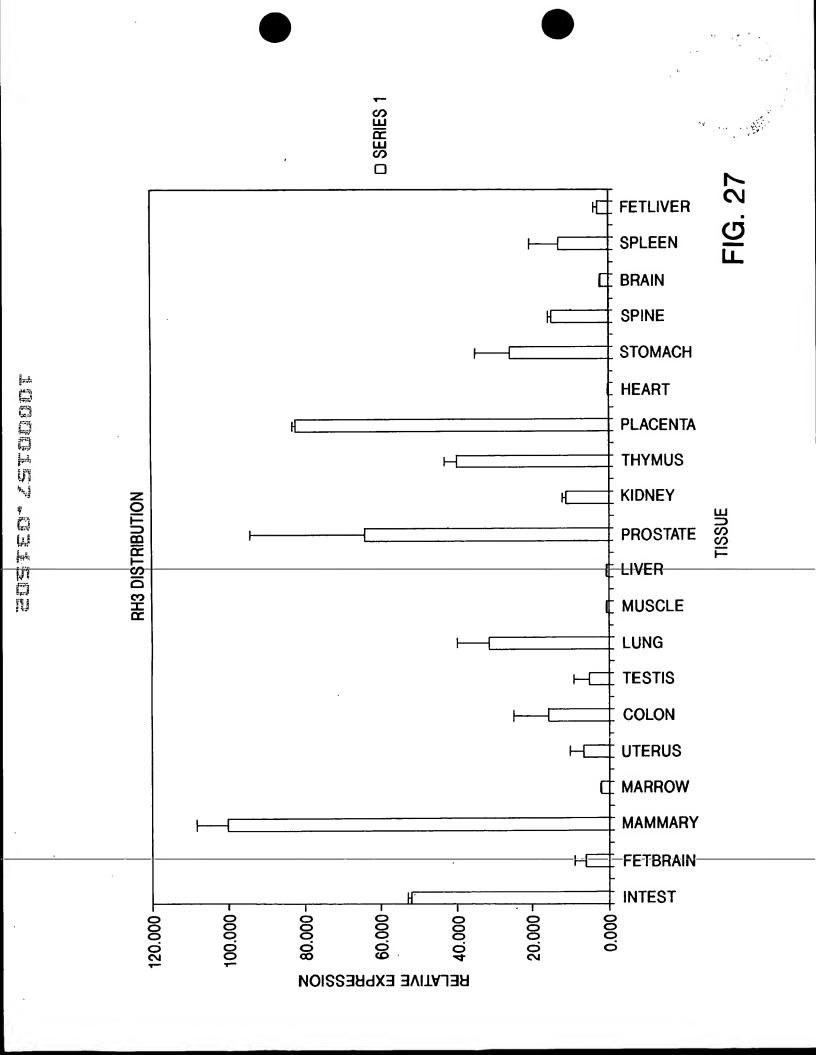
HEART
HEART
KIDNEY
LIVER
LUNG
COLON
MARROW
INTESTINE
SPLEEN
STOMACH
THYMUS
PROSTATE
MUSCLE
TESTIS
UTERUS
FETAL BRAIN
FETAL LIVER
SPINAL CHORD
PLACENTA
ADRENAL
PANCREAS
SALIVARY
TRACHEA

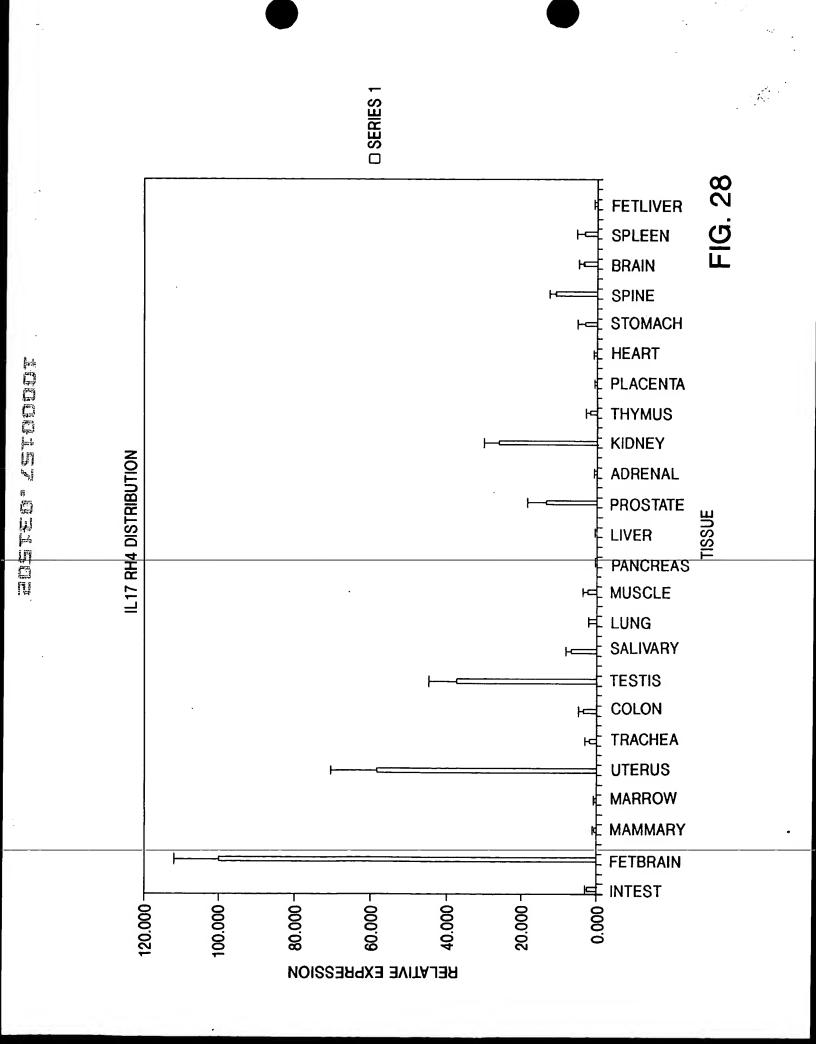
FIG. 23











Sag.

h-IL17 h-IL17B h-IL17C h-IL17E	1 MTPGKTSLVSLLLLLSLEAIVKAGITIPR MDWPHNLLFLLT	
h-1L17 h-1L17B h-1L17C h-1L17E	30 N PGCPNSEDKNFPRTVMVNLNIHNRNTN 39 A PGPHQVPLDLVSRMKPYARMEEYERNIEEMVAQLRNSSE 47 A PPHLLARGAKWGQALPVALVSSLEAASHRGRHERPSATT 42 SKGQDTSEELLRWSTVPVPPLEPARPNR	TNPKR CLAQRKCEVNL QCPVLRPEEV HPESCRASE -
h-IL17 h-IL17B h-IL17C h-IL17E	63 - SSDYYNRSITSPWNLHRNEDPERYPSVIWEAKCRHLGCIN 89 QLWMSNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGCVN 97 LEADTHQRSISPWRYRVDTDEDRYPOKLAFAECLCRGCID 79 - DGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVS	ADG N V D Y H P F T M Q E D R S M A R T G - R E T A A L Q T G S H M D P R
h-IL17 h-IL17B h-IL17C h-IL17E	110MNS VP 1 QQE 1 LV L R R E PPHCPN SF R L EKTLV 139V S V P V F SQV P V R R R L C PP P PR T G P C R Q R A V M E T 1 146L N S V R L L Q S L L V L R R R P C S R D G S G L P T P G A F A F H T E F T H V 128G N S E L L Y H N Q T V F Y R R P C H G E K G T H K G Y C L E R R L Y R V	SVGCTCVTP   AVGCTCVTP   PVGCTCVLP   SLACVCVRP
h-IL17 h-IL17C h-IL17E	151 <mark>V</mark> ) Н Н V А 196\$ V 175V M G	

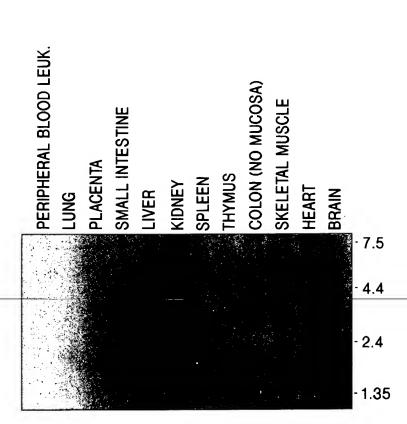


FIG. 31A

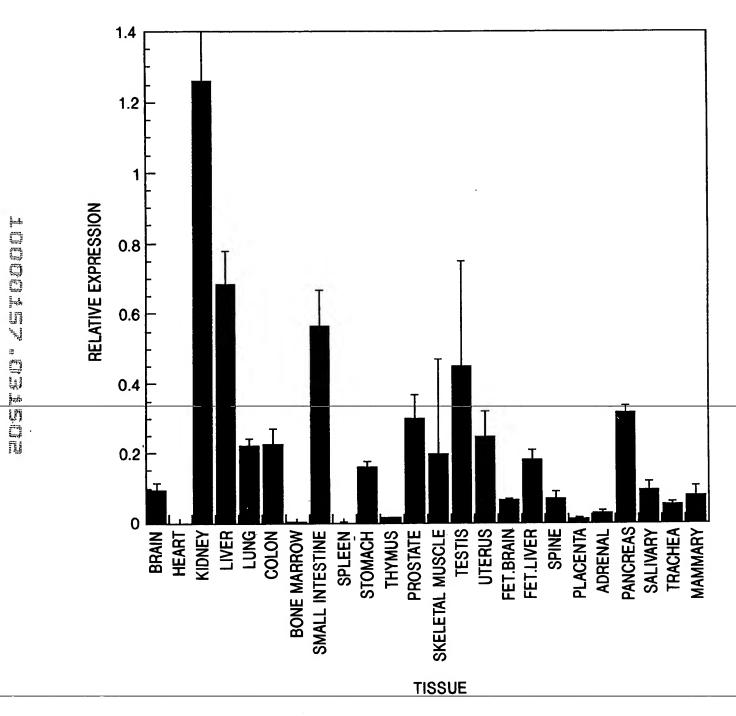


FIG. 31B

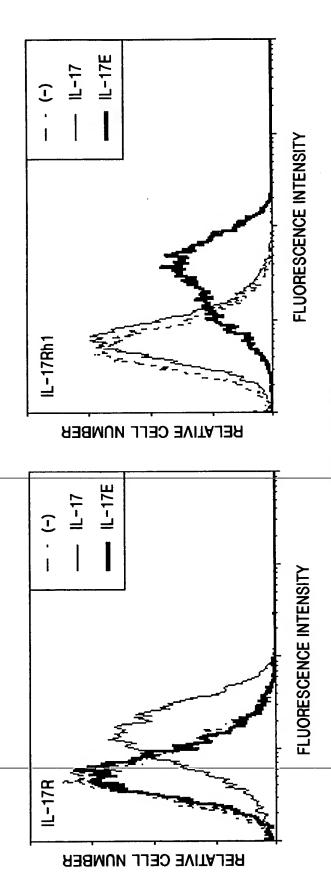


FIG. 32A

FIG. 32B

ķ.,

i

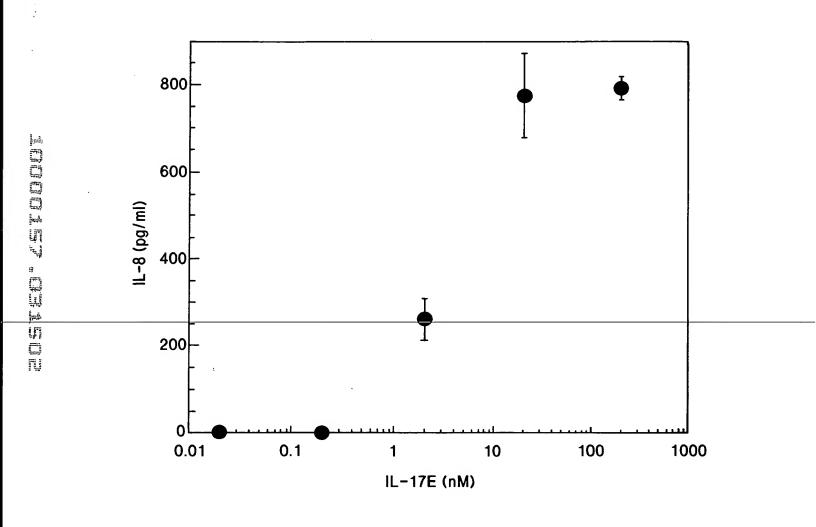


FIG. 34

## IL-17 FAMILY OF CYTOKINES HAS COMPLEX PATTERN OF OVERLAPPING RECEPTOR-LIGAND SPECIFICITIES

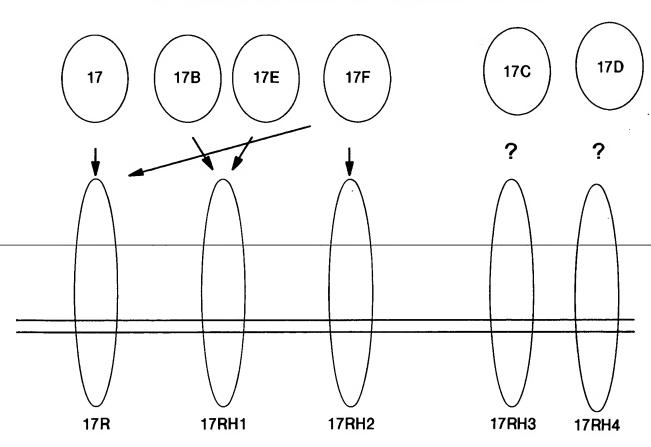
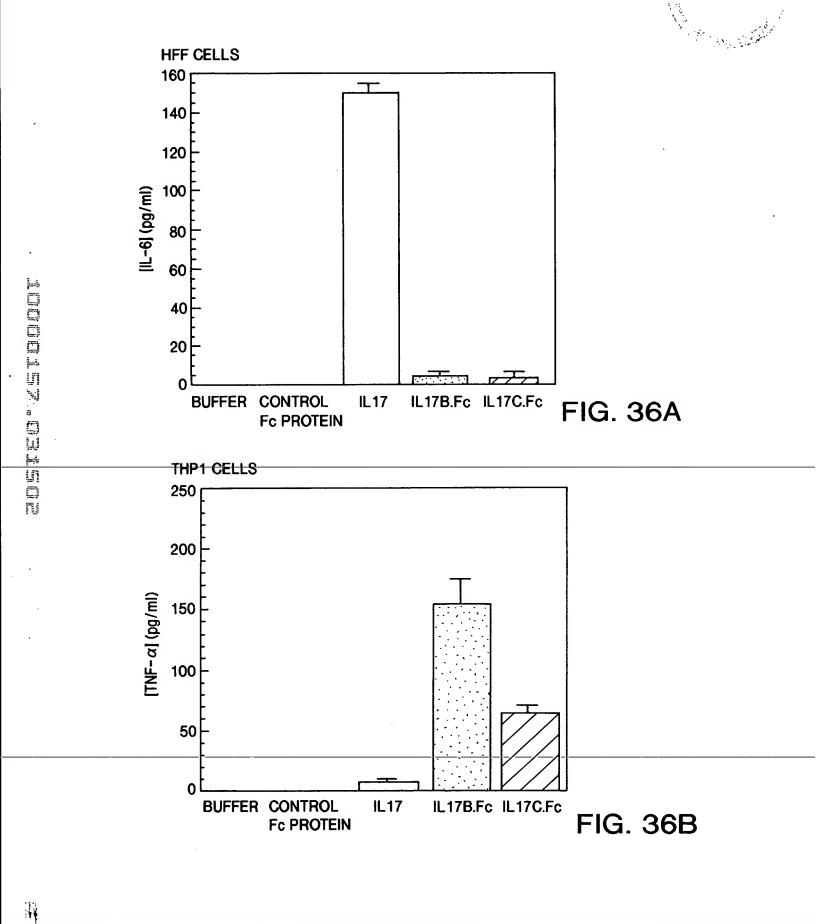
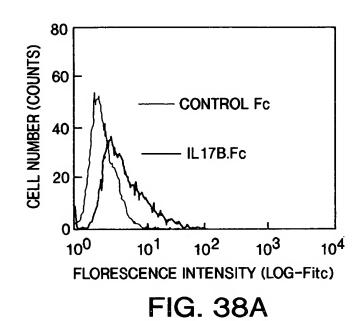


FIG. 35



i.



SO CONTROL FC

40

100

101

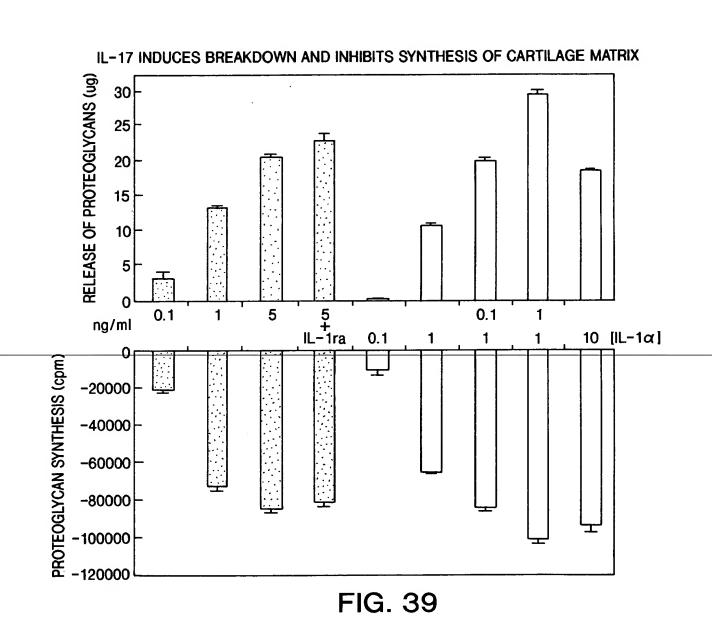
102

103

104

FLORESCENCE INTENSITY (LOG-Fitc)

FIG. 38B



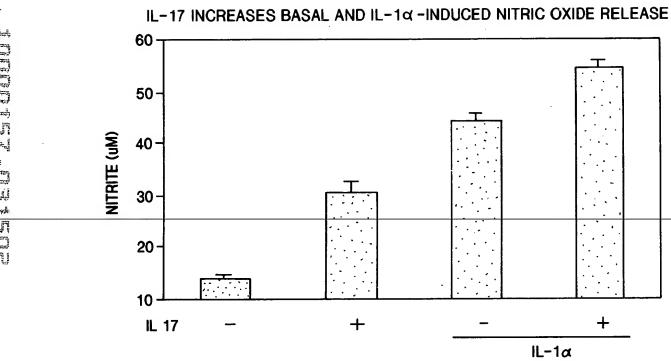
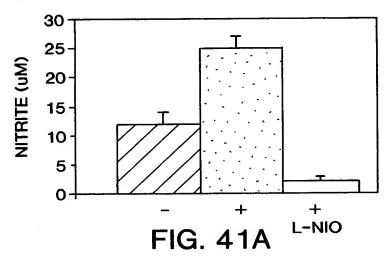
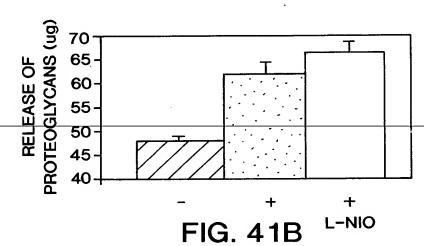
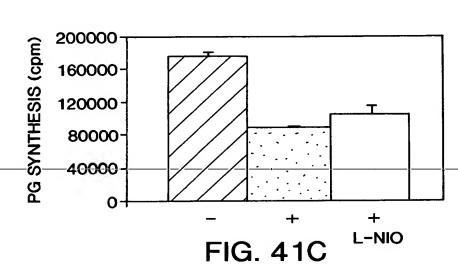


FIG. 40

## INHIBITION OF NITRIC OXIDE RELEASE DOES NOT BLOCK THE DETRIMENTAL EFFECTS OF IL 17 ON MATRIX BREAKDOWN OR SYNTHESIS







SYNTHESIS OF PGs (cpm)

## INHIBITION OF NO RELEASE ENHANCES IL 1- $\alpha$ -INDUCED MATRIX BREAKDOWN BUT NOT MATRIX SYNTHESIS

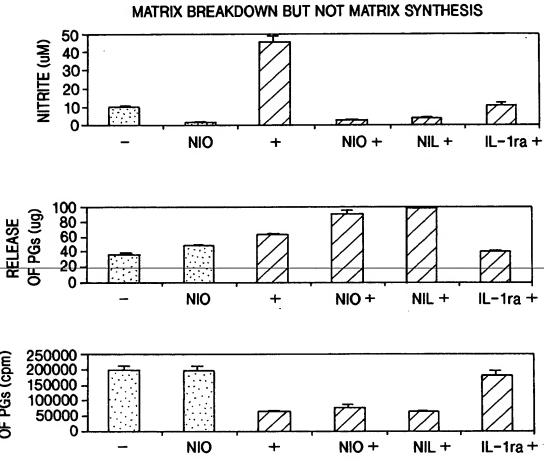
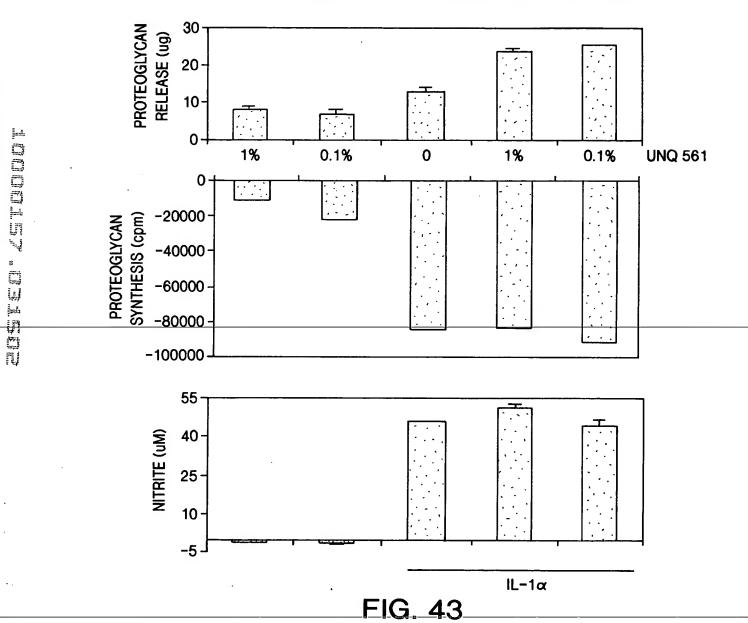
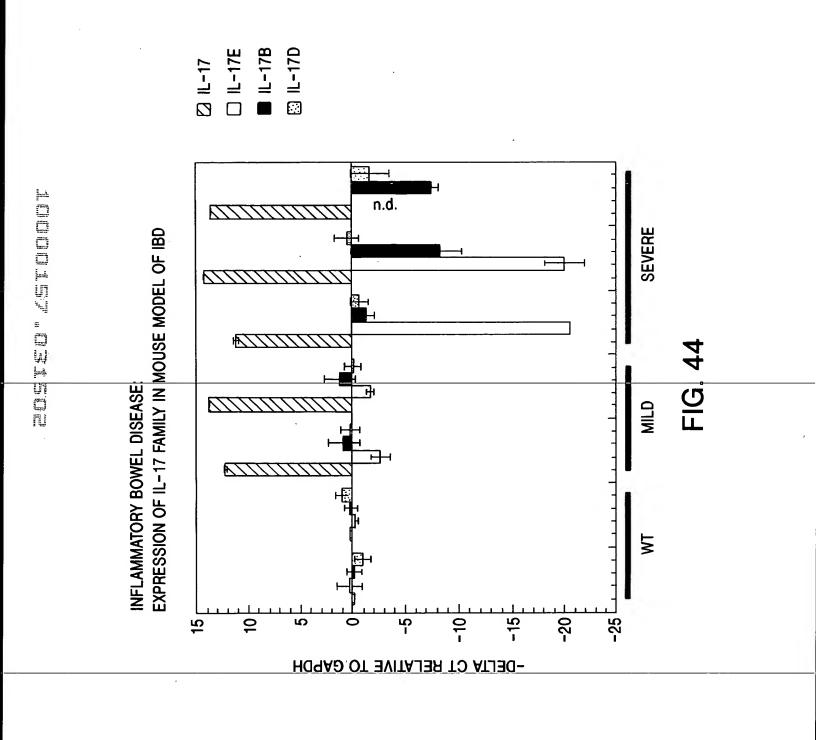
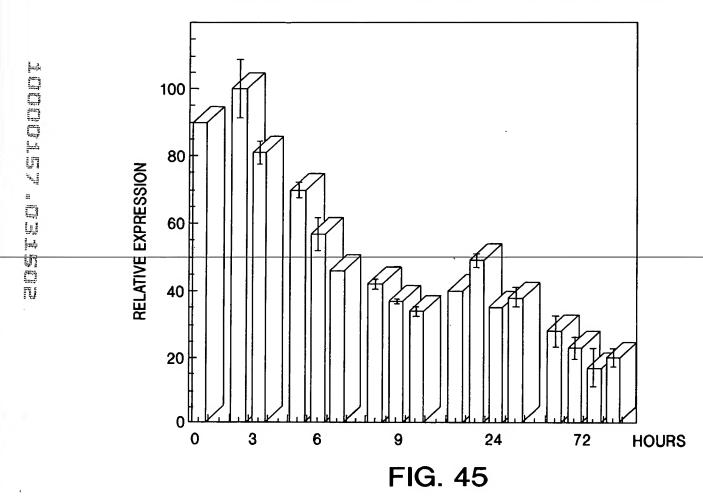


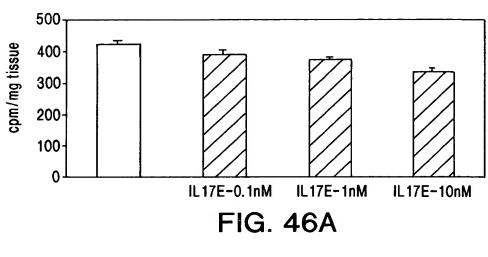
FIG. 42

### IL-17C DETRIMENTAL EFFECTS ON ARTICULAR CARTILAGE









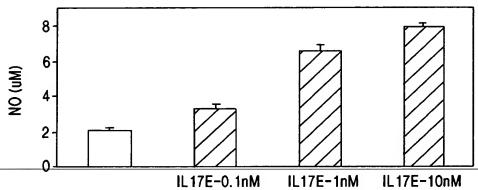


FIG. 46B

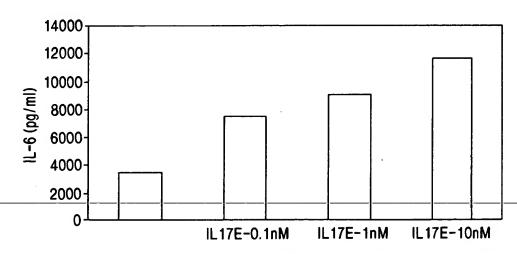
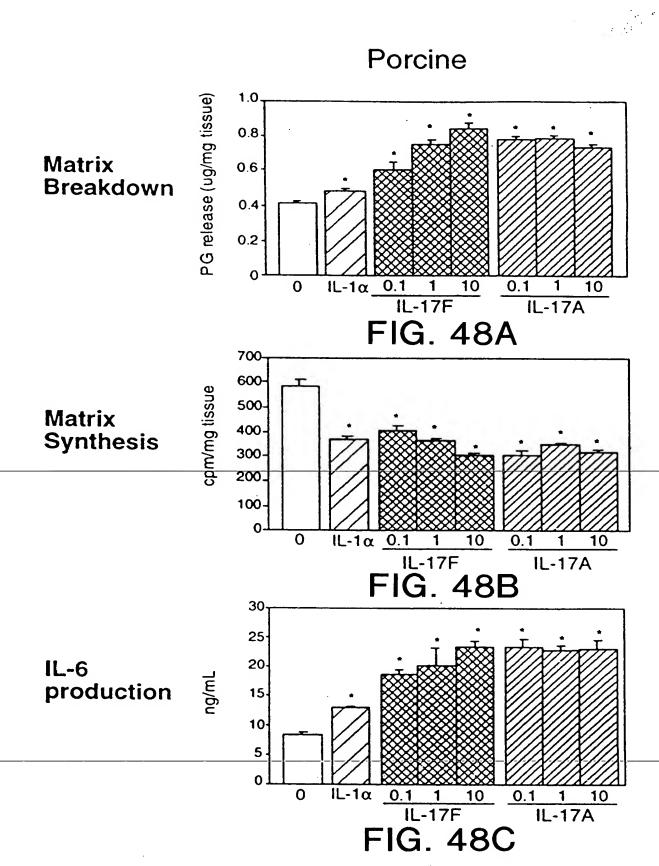
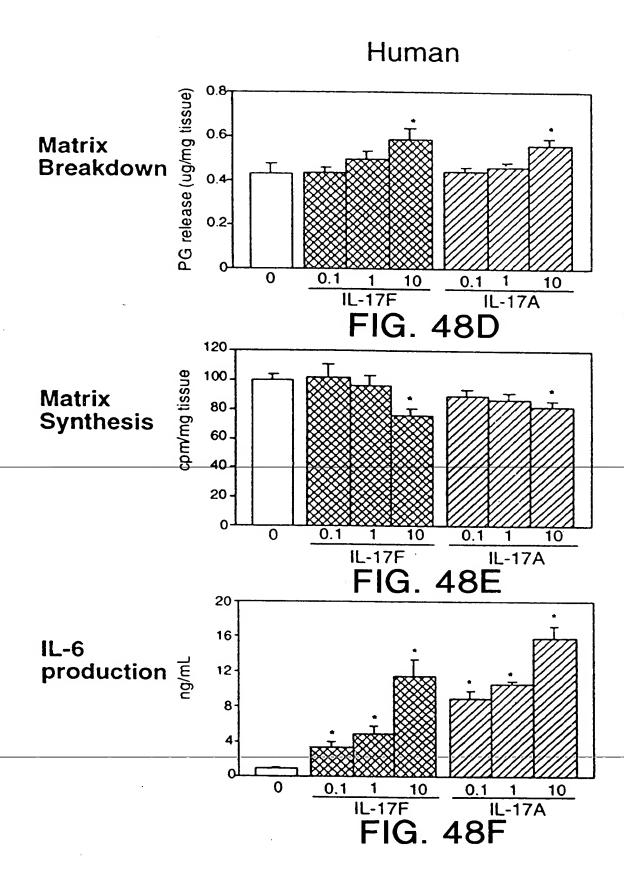


FIG. 46C





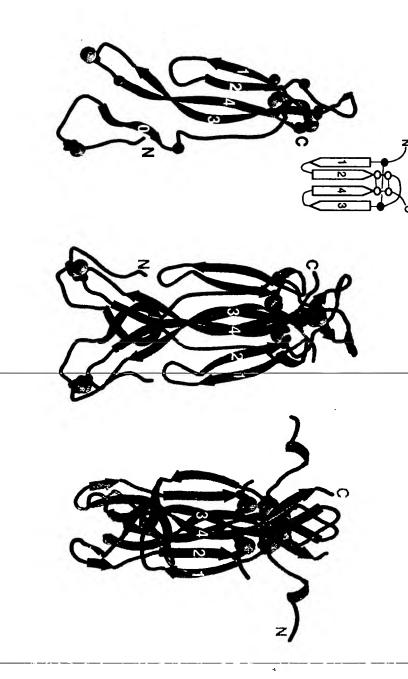


FIG. 49A

FIG. 49B

FIG. 49C

					*	•
IL-17A IL-17B IL-17C	QPRS HHDPSLRGHP	HSHGTPH YS	PGPLAPGPHQ AEELPLGOAP	PHLLARGAKW	ITIPRNP.G PYARMEEYER GOALPVALVS	14 44
IL-17F	PPVPGG	EMELDI.	GT INTENDDUG	WORN THE COM		
IL-17A	PNSEDKNFPR	TVMVNINTHN	BULLINAM DE	POGNYVNDGM	PWNITVIWD	59
IL-17B	NIEEMVAQLR	NSSELAOR	KARV. NT.	VERDITIEST.	PWOVETAWN	62 88
IL-17C	SLEAASHRGR	HERPSATT	OSPVIRPERV	T.RAINTHORET	- ENGISIME	98
IL-17E	STVPVPPLEP	. ARPNRHPE	S-RASE	DGPI.NSRAT	DWDVFIDDD	65
IL-17F	PNRYPSEVVQ	AQ RNLG IN	AQGKEDIS	MN VPI.QOE	TLVVRRKHOG	106
IL-17A	PERYPSVIWE	AK RHLG IN	A. DGNVDYH	MN VPT OOF	TI.VI.PPEDDU	100
IL-17B	PSRIPVDLPE	AROLOLGOVN	PF. TMOEDRS	MV VDV FGO	TENTED T.	122
1F-14C	EDRYPOKLAF	AE & L & RG & ID	AR TGRETAA	LN VRL TOR	TIVIDD DD	1 4 4
IL-17E	LNRLPQDLYH	ARELEPHIVS	LQTGSHMDPR	GN ELLYHNQ	TVFYRRP	112
	*		A all the state of	in the second se		
IL-17F	gsv	SFQLEK	VLVIVGER	CALBAIHHAO	• • •	133
IL-17A	EPN	SFRLEK	ILVSVGET	CVTPIVHHVA	• • •	136
	CPPPPRTGP.	RORA	VMETIAVGET	GTP		160
	SRDGSGLPT	PGAFAFHTEF	IHVPVG3T	CV.LPRSVAA	ALE	184
IL-17 <b>E</b>	CHGEKGTHKG	LER	RLYRVSLAOV	EVRPRVMG.		145

FIG. 50

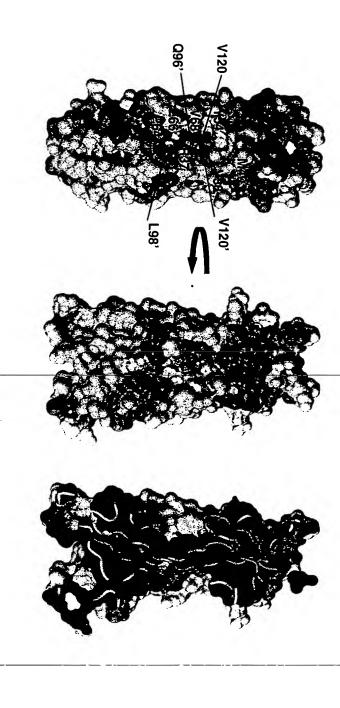


FIG. 51A

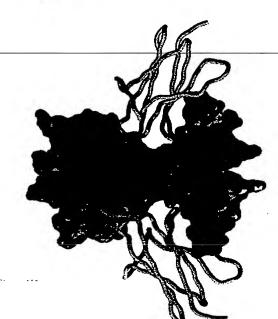
FIG. 51B

FIG. 51C

FIG. 52C

FIG. 52A

FIG. 52B



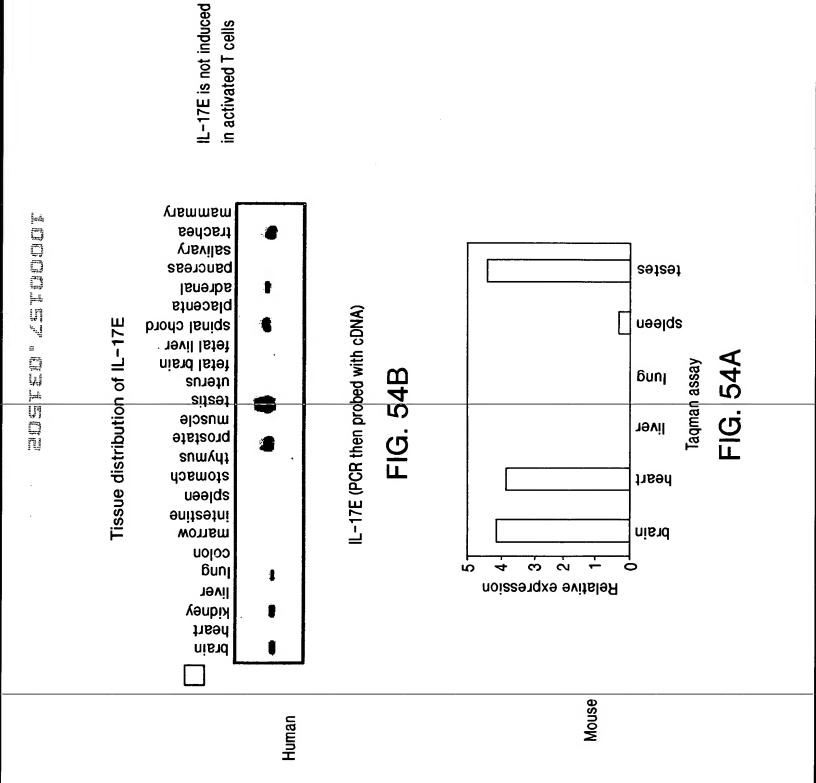
# IL-17E is highly conserved between human and mouse

SHWPSCCPS ---VAFLAMIVGTHTVSLRIQEGCIND X - - - -SLISLFLQVVAFLAMVMGTHT ß GED MRERPRL mlL-17E hL-17E 35 KEQEPPEEWLKWSSASVSPPEPLSHTHHAESCRASKDGPLNSRAISPWSY 43 KGQDTSEELLRWSTVPVPPLEPARPNRHPESCRASEDGPLNSRAISPWRY mL-17E NL-17E

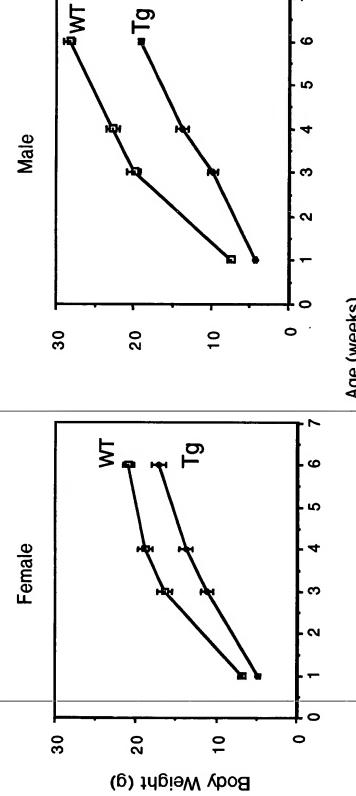
93 ELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDPRGNSELLYHNQTVFYR 85 ELDRDLORVLORVPQDLYHARCLCPHCVSLQTGSHMDPLGNSIVPLYHNQTVFYR mlL-17E ML-17E

135 RPCHGEEFTHR RYCLERKLYKVSLACVCVKPKVMA G THK GY CLERRLY RV SLACVCVRPRVMG 143 RPCHGEK mL-17E NL-17E

FIG. 53







Age (weeks)

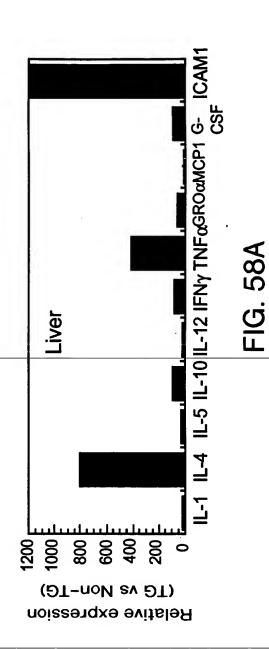
FIG. 55

IL-17E transgenics are jaundiced by 6 weeks of age



**X** 

FIG. 56



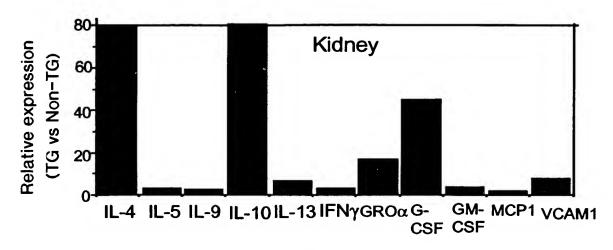


FIG. 58B

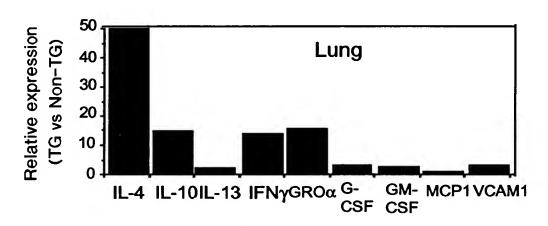
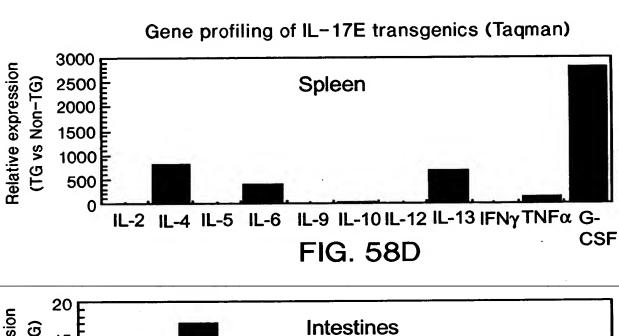


FIG. 58C



Intestines

Intestines

IL-1 IL-4 IL-5 IL-9 IL-10 IL-12 IFNy TNF \( \alpha \) GRO\( \alpha \) MCP1 VCAM1

FIG. 58E

,,)



# Elevated serum IL-5, IL-13 and TNF $\alpha$ in mIL-17E transgenics

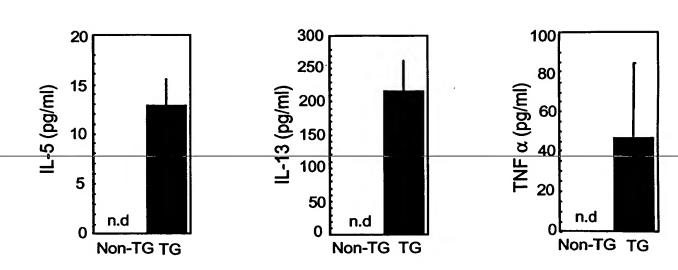


FIG. 60

# Serum IgE and IgG1, but not IgG2a is elevated in mIL-17E transgenics

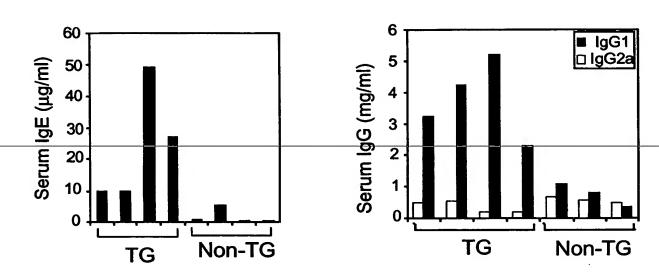
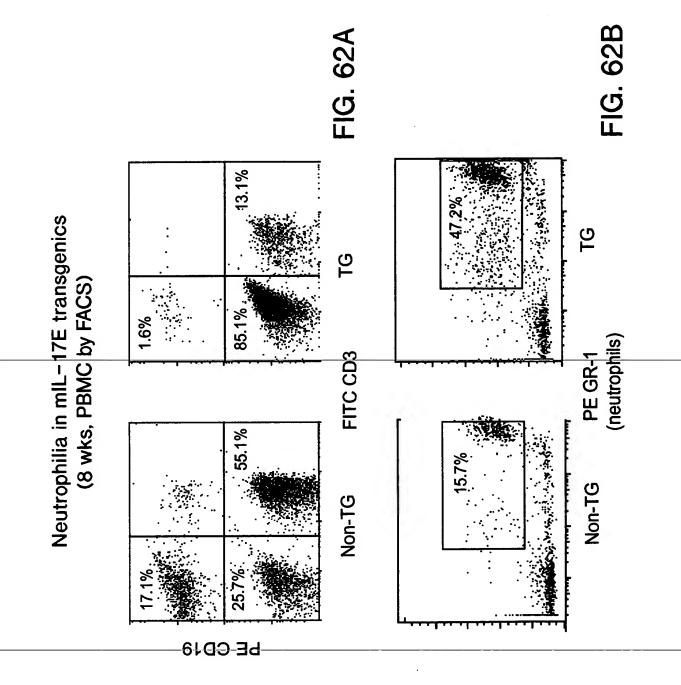


FIG. 61



# Neutrophilia and eosinophilia in mIL-17E transgenics (hematology)

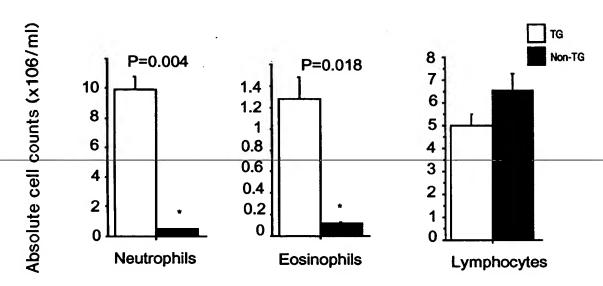


FIG. 63

# G-CSF is elevated in mIL-17E transgenics

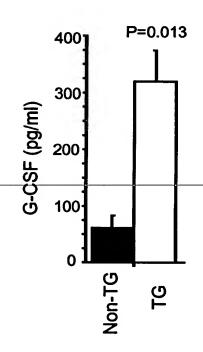


FIG. 64

IL-17E induces production of G-CSF in vitro

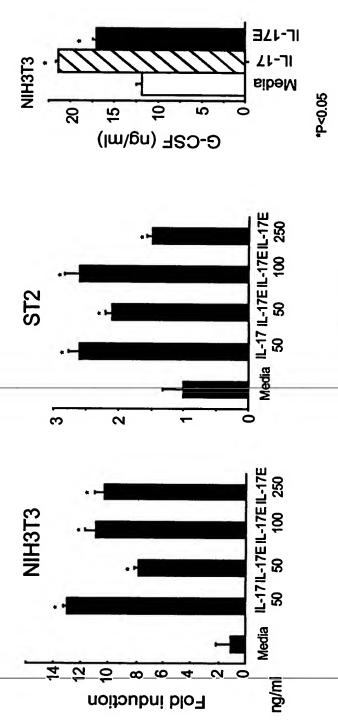
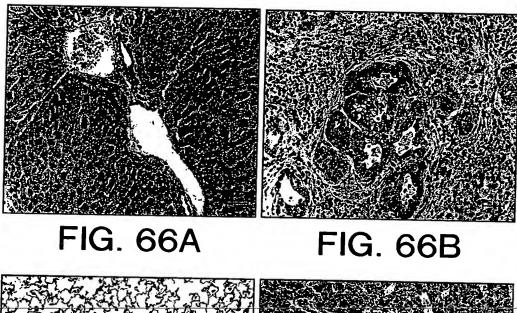


FIG. 65



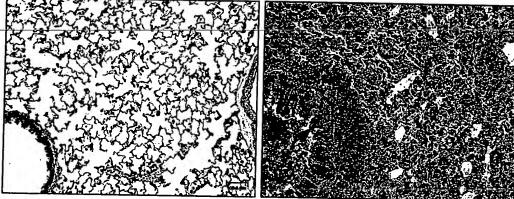


FIG. 66C

FIG.66D